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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

WEHBE, ANNE MARIE SABRINA

ART UNIT	PAPER NUMBER
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1633

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/780,114

Applicant(s)

DOW ET AL.

Examiner

Anne Marie S. Wehbe

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) 23 and 25-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-22, 24 and 29-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's response to the restriction requirement, received on 11/14/06, has been entered. Applicant's election of the species of nucleic acid "a) a nucleic acid without a gene insert" without traverse is acknowledged. Applicant's further election of the species of cytokine "c) IFN-gamma" with traverse is also acknowledged. The traversal is on the grounds that the applicant has claimed three species of cytokine which the applicant contends is a reasonable number of species. This is not persuasive since the genus of cytokines includes far more than 3 species. The instant specification for instance identifies 9 cytokines on page 21. Further, the genus of cytokines comprises more than 9 different cytokines- for instance, the interleukin family of cytokines alone has more than 21 different members. It is also noted that the claims are limited to the three cytokines referred to by applicant. Claim 17 is generic to any cytokine. Thus, the traversal is not persuasive and the election of species requirement for the genus of cytokines is maintained and made FINAL.

Claims 1-34 are pending in the instant application. Of these, claims 23, and 25-28 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Claims 1-22, 24 and 29-34 are currently under examination based on applicant's elected species of a vector without a gene insert and IFN-gamma. An action on the merits follows.

Priority

The applicant's claim for benefit of priority to parent application 09/104,759 is acknowledged. However, while the specification on page contains an appropriate statement of priority referring to this parent application, the reference does not include the status of the parent application. 09/104,759 has issued as U.S. Patent No. 6,693,086. The applicant is required to amend the specification to insert the status of the 09/104,759 application.

Duplicate Claims

Applicant is advised that should claim 21 be found allowable, claim 22 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Double Patenting

Claims 1-8, 10-22, 24 and 29-34 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-18 of U.S. Patent No. 6,693,086, hereafter referred to as the '086 patent. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

The claims of the '086 patent are both broader and narrower than the instant claims. The '086 claims are drawn to a method of eliciting a non-antigen specific immune response in a

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mammal by administering a composition comprising cationic liposome delivery vehicle and an isolated bacterially derived nucleic acid vector without a gene insert. The '086 patent claims are narrower than the instant claims in that they are limited to bacterially derived vectors and cationic liposomes, whereas the instant claims more broadly recite a liposome delivery vehicle and a vector without a gene insert. In this respect, the '086 claims are a species of the instant claims and so render the instant claims obvious. However, the '086 claims are also broader than the instant claims in that they do not recite specific routes of administration such as intravenous or intraperitoneal administration, nor do they specifically recite that the non-antigen specific immune response is therapeutic for any specific condition, such as cancer, a viral infection, or allergy. The '086 claims also do not teach the inclusion of a nucleic acid encoding a cytokine in the composition. However, the '086 claims broadly encompass these specific embodiments and the specification of the '086 patent specifically teaches each of these limitations, see columns 9, and 16, for teaching that the non-antigen specific immune response treats cancer, infectious disease including viral infection, and allergic inflammation, see columns 11-13 for routes of administration which include intravenous and intraperitoneal, and see columns 14 and 21 for including a nucleic acid encoding a cytokine in the composition. Therefore, while broader than the instant claims, the '086 claims fully encompass the specific embodiments recited in the instant claims. Thus, the combination of the '086 claims and the teachings of the '086 specification render obvious the instant methods as claimed.

Claim Rejections - 35 USC § 112

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-22, 24 and 29-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for eliciting a systemic, non-antigen specific immune response in a mammal, comprising administering to said mammal an amount of a composition comprising a cationic liposome delivery vehicle and an isolated bacterially-derived pCR3.1 vector without a gene insert, does not reasonably provide enablement for said methods of eliciting a systemic, non-antigen specific immune response using any liposome delivery system and any nucleic acid vector without a gene insert, or for using said methods to treat any viral infection, cancer, or allergic condition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The specification fails to provide sufficient guidance for mammalian, viral, insect, or bacterial nucleic acid vector sequences without a gene insert which are capable of stimulating systemic, non-specific immune responses capable of treating conditions such as cancer, viral infections, and allergic inflammation. The specification fails to adequately describe actual mammalian, insect, viral, or bacterial nucleic acid sequences which are immunostimulatory other than the pCR3.1 plasmid, and salmon sperm or calf thymus DNA. In particular, the only actual bacterial immunostimulatory sequence disclosed by the specification is the empty pCR3.1 vector, and the specification does not particularly describe which sequence or sequences in this

vector are responsible for its immunogenicity. The art at the time of filing teaches that unmethylated CpG motifs in bacterial DNA can be immunostimulatory. However, not all bacterial DNA sequences are immunostimulatory even in the context of liposome mediated delivery. Huang et al. for instance teaches that delivery of empty pcDNA vectors with liposomes fails to affect immune responses associated with allergic inflammation (U.S. Patent No. 6,121,247, 9/19/00, Huang et al., Figure 5, a-d). Furthermore, in regards to viral or mammalian nucleic acid sequences, the specification only discloses salmon sperm DNA, and calf thymus DNA. Both of these embodiments comprise the full chromosomal DNA content of salmon sperm, or a calf thymus and are as such do not qualify as a vector without a gene insert. The specification does not teach which sequences within the sheared mammalian chromosomal DNA are actually immunostimulatory or how to use such sequences to construct a vector without a gene insert capable of inducing non-antigen specific systemic immunity. In addition, it is noted that because both salmon sperm DNA and calf thymus DNA are simply sheared chromosomal DNA, it is not clear which fragments of the DNA are actually responsible for stimulating non-specific immunity. In the absence of any particular evidence, it is possible that fragments of the DNA are actually expressed following administration in vivo, since the genomic DNA contains both large and small fragments which may include complete genes or expressible fragments thereof. In addition, the specification itself teaches that at the time of filing, it was established in the art the DNA from eukaryotic sources is not stimulatory, citing a number of references, see page 55 in the specification.

Therefore, based on the enormous number of nucleic acid vector sequences encompassed by applicant's claims, the lack of adequate description of actual immunostimulatory nucleic acid

sequences derived from any source or guidance as to how such sequences can be used to construct a vector which retains immunostimulatory properties, the nature of the invention and the state of the art regarding the characteristics of immunostimulatory DNA sequences, and the limitations of the working examples to a single vector without a gene insert, an empty pCR3.1 plasmid, it would have required undue experimentation to practice the scope of applicant's invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 17-18 depend on claim 1, which recites a method of administering a composition comprising a liposome delivery vehicle and a vector without a gene insert, i.e. an empty expression vector. Claim 17 recite wherein the composition further comprises a recombinant nucleic acid molecule having a nucleic acid sequence encoding a cytokine. Based on the limitation of claim 1, that the vector does not have a gene insert, it is unclear whether the applicant now intends to encompass a vector comprising the recombinant nucleic acid which express the cytokine, or whether the applicant intends that the vector without a gene insert is separate from the nucleic acid encoding the cytokine. Clarification is requested. If applicant intends to claim a composition with three separate elements, i.e. the liposome, a first vector

without a gene insert, i.e. an empty vector, and a second separate expressed nucleic acid, it is suggested that applicant amend the claim to more definitely reflect this aspect of the invention.

Claim Rejections - 35 USC § 103

Claims 1, 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,121,247 (9/19/00), hereafter referred to as Huang et al., in view of U.S. Patent No. 5,830,878 (11/3/98), hereafter referred to as Gorman et al. The applicant claims methods of eliciting a systemic, non-specific immune response comprising administering by intravenous or intraperitoneal injection a liposome delivery vehicle, a vector without a gene insert, and a nucleic acid encoding a cytokine. The claims further recite wherein the cytokine is interferon-gamma. Although, claim 1 recites a vector without a gene insert, claims 17-18 which depend on claim 1 recite that the composition further comprises a nucleic acid encoding a cytokine. As indicated in the above discussion of claims 17-18 under 35 U.S.C. 112, second paragraph, it is unclear whether the nucleic acid encoding the cytokine is part of the vector or separate. As such, in the interests of compact prosecution, the following rejection applies to the embodiment of claims 17-18 which appears to encompass a single vector encoding a cytokine.

Huang et al. teaches the prevention and therapy of allergic inflammation in the lung comprising the administration of liposomes and a plasmid DNA encoding interferon-gamma operatively linked to expression control elements (Huang et al., columns 9-10, claims 1-8). While Huang et al. does not explicitly state that the administration results in “non-specific immune responses”, “When the structure recited in the reference is substantially identical to that

of the claims, claimed properties or functions are presumed to be inherent.” See MPEP 2112.01 or *In re Best*, 195 USPQ 430, 433 (CCPA 1997). Please note as well that reliance upon inherency is not improper even though rejection is based on Section 103 instead of Section 102. *In re Skoner*, et al. 186 USPQ 80 (CCPA).

Huang et al. differs from the instant invention by not specifically teaching intravenous or intraperitoneal administration of the liposomes and plasmid DNA encoding interferon-gamma. Gorman et al. supplements Huang et al. by teaching methods of introducing a recombinant expression construct to a cell within a lung comprising the intravenous administration of cationic liposomes and a recombinant expression construct (Gorman et al., column 23, claim 4). Gorman et al. also supplements Huang et al. by teaching various compositions of liposomes and plasmid DNA, including DOTIM and DOTAP and cholesterol, and the production of multilamellar vesicle lipids (Gorman et al., columns 5-9). Based on the successful targeting and transfection of lung cells using intravenous injection taught by Gorman et al., the skilled artisan would have been motivated to utilize intravenous administration to administer the liposomes and plasmid DNA encoding interferon-gamma in the method of treating allergic inflammation in the lung taught by Huang et al. Based on the fact the either intravenous or local administration of liposomes and plasmid DNA to lung cells results in expression of the plasmid DNA in the lung, it would have been *prima facie* obvious to the skilled artisan to substitute intravenous injection of liposomes and plasmid DNA encoding interferon-gamma for the local delivery taught by Huang et al. in order to treat allergic inflammation in the lung with a reasonable expectation of success.

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No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197.

Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to be 'AMW', with a long horizontal line extending from the right side of the signature.